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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,159	05/03/2001	Yang-Dar Yuan	D2977	7424

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EXAMINER
HUI, SAN MING R

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 06/02/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/848,159	YUAN ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *7-10,13-15 and 17-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,11,12,16 and 22-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14, 16* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's response filed December 23, 2002 is acknowledged. No claims are amended.

Claims 1-26 are pending.

Claims 7-10, 13-15, and 17-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Claims 1-6, 11, 12, 16, and 22-26 have been examined herein to the extent they read on the elected species, AGN 194310 (also known as 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 11, 12, 16, and 22-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, there is no support found in the originally filed specification or claims for the herein recited limitation "to treat hyperlipidemia caused other than by the administration of retinoids to the mammal". Applicant remarks that support would be found on page 6, lines 15-18 and Examples 1-7 on pages 23-27.

These applicant's rebuttal arguments regarding the disclosed pages have been considered but are not found persuasive. There is no specific disclosure directed to a specific cause of hyperlipidemia found in these pages. Examples 1-7 also do not specify disclose a specific cause of the hyperlipidemia in the patients tested.

The new matter recited in the claims, as stated above, are not examined on the merits herein.

Response to arguments with regard to new matter rejection

Applicant's arguments filed December 23, 2002 averring the instant invention not require the coadministration of retinoid have been considered, but are not found persuasive. Examiner notes that the basis of the new matter rejection is not because the specification fails to describe the coadministration of retinoid and the compounds herein. The arguments are apparently not related to the ground of rejection set forth in the previous office action.

Applicant's arguments filed December 23, 2002 averring the specification clearly and properly describes the herein recited limitations have been considered, but are not found persuasive. Examiner notes that there is no description in the instant specification with regard to the cause of hyperlipidemia. The background of the invention in the instant specification discloses what hyperlipidemia and its consequences are. The background of the invention in the instant specification also discloses what treatments of hyperlipidemia are currently available. The detailed description Section also fails to discuss or disclose the cause of hyperlipidemia. The detailed description Section merely discuss the activities of RAR and RXR in the cellular

level, without relating to the pathophysiology of hyperlipidemia. Afterwards, it discloses: "It is surprisingly discovered that the administration of a composition comprising an RAR antagonist or an RAR inverse agonist to a mammal lowers its lipid concentration" in page 5 of instant specification. In other words, there is no disclosure in the instant specification teaching the cause of specific cause of hyperlipidemia, neither expressly nor implicitly. However, the instant claims specifically exclude one specific cause of hyperlipidemia. Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977). See also MPEP 2163 and 2173.05(i).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 11, 12, 16, 22-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klein et al. (US Patent 5,776,699) in view of Aberg et al. (Atherosclerosis, 1985; 54:89-97), references of record in the previous office action mailed October 2, 2001.

Klein et al. teaches a group of RAR antagonists broadly, including the elected compound AGN 194310, being useful in inhibiting hypertriglyceride (See particularly Col. 3, line 45-col. 4, line 49; also col. 20, line 67).

Klein et al. does not expressly teach the employment of 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid specifically in the method of lowering triglyceride. Klein et al. does not expressly teach the employment of 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid to prevent myocardial infarction.

Aberg et al. teaches that elevated serum triglyceride is one of the risk factor of developing myocardial infarction (See particularly page 89, third para.; also page 93, Table 1 and page 95, Table 3).

It would have been obvious to one skill in the art when the invention was made to employ AGN 194310 in a method to lower triglyceride level and prevent myocardial infarction.

One of ordinary skill in the art would have motivated to employ 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid in a method of lowering triglyceride level and preventing myocardial infarction because the RAR antagonists of Klein et al. are known to be useful in inhibiting hypertriglyceridemia. Therefore, employing any RAR antagonists of Klein et al., including 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid, would have been reasonably expected to be useful in a method of lowering triglyceride level. Furthermore, it is known that elevated serum triglyceride increasees the risk of

developing myocardial infarction in patients. Therefore, patients taking 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid to lower their serum triglycerides level would be reasonably expected to prevent the development of myocardial infarction.

Response to Arguments

Applicant's remarks regarding the recitation of the new matter have been considered moot because the new matter limitations, as discussed above, are not examined on the merits.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
May 28, 2003

SREENI PADMANABHAN
PRIMARY EXAMINER

6/1/03